Can Low PCT Levels Identify LRTI Patients Unlikely to Benefit From Antibiotic Therapy?

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Tsalik EL, Rouphael NG, Sadikot RT, *et al.*
Efficacy and safety of azithromycin versus placebo to treat lower respiratory tract infections associated with low procalcitonin: a randomised, placebo-controlled, double-blind, non-inferiority trial.
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The TRAP-LRTI trial aimed to compare the efficacy and safety of azithromycin versus placebo to treat lower respiratory tract infections (LRTIs) in patients with low procalcitonin (PCT) levels.

Bacterial and viral LRTIs have similar clinical manifestations resulting in high rates of inappropriate antibiotic utilization. Investigators hypothesized that patients with suspected non-pneumonia LRTI and a procalcitonin concentration of 0.25 ng/mL or less are unlikely to have a bacterial infection, and hence, would not benefit from antibiotics.

TRAP-LRTI study design:

- Randomized, placebo-controlled, double-blind, non-inferiority trial
- Conducted at 5 health centers in the USA between December 8, 2017 and March 9, 2020
- Adults aged ≥18 years with clinically suspected non-pneumonia LRTI & symptom duration from 24 h to 28 days were enrolled at clinics or emergency departments
- Participants (n=499) with a PCT concentration of ≤ 0.25 ng/mL received (1:1) oral azithromycin 250 mg (n=249) or matching placebo (n=250)

Primary outcome: efficacy of azithromycin vs. placebo (clinical improvement at day 5 in intention-to-treat population)

Day 5: placebo was not non-inferior to azithromycin in terms of clinical improvement
Day 11: placebo was non-inferior to azithromycin
Day 28: mixed findings. Placebo was not non-inferior to azithromycin in the intention to treat group but was non-inferior to azithromycin in the per-protocol group.

Secondary outcome: solicited adverse events
Placebo group showed better outcomes using the DOOR-RADAR* analysis that accounted for azithromycin-related solicited adverse events and the inherent harms of unnecessary antibiotic use.

In conclusion, at day 5, it is unclear whether antibiotics are indicated for patients with LRTI and a low PCT concentration. However, at later timepoints**, low PCT levels were shown to safely identify adults with LRTI who are unlikely to benefit from antibiotic therapy**, especially when accounting for the harms associated with unnecessary antibiotic use.

"Clinicians should weigh these factors (clinical improvement, reduced adverse events, and lower antibiotic use) when deciding whether to use procalcitonin as a guide for antibiotic initiation," concluded the study authors.